

**REMARKS**

Applicants have now had an opportunity to carefully consider the Examiner's comments set forth in the Office Action mailed December 20, 2005.

Reconsideration of the Application is requested.

Claims 1-7 are pending in the application. Claim 1 is amended. Claims 5 and 6 currently stand withdrawn, but claim 5 has been amended, and claim 6 depends from claim 5. New claim 7 is added.

**The Office Action**

**Election Requirement**

Applicants confirm their election of Group I, claims 1-4, drawn to a magnetic marker. Claim 5 has been amended to depend from claim 1. Accordingly, it is respectfully requested that should an allowable claim be found, claims 5-6, drawn to a method of making a magnetic marker, be rejoined.

**35 USC §102(b) and §103(a) Rejections**

Claims 1 and 2 were rejected under 35 USC §102(b) as being anticipated by Colin, et al., U.S. Patent 5,773,307.

Claims 3 and 4 were rejected under 35 USC §103(a) as being unpatentable over Colin, et al., U.S. Patent 5,773,307.

For the reasons outlined below, it is submitted that the claims are now in condition for allowance.

Claim 1 now recites a magnetic marker composed of a magnetic fine particle which exhibits residual magnetism and a polymer encapsulating the particle, for use in measuring an immunoreaction with a SQUID magnetic sensor. The particle diameter of the magnetic fine particle is 20 to 40 nm and the external diameter of the magnetic marker is 40 to 100 nm. The polymer has carboxyl groups on the surface thereof.

Support for the amendments to claim 1 is found in the specification (pg 6, lns15-18).

The present inventors have discovered that the size (the diameter) of magnetic fine particles encapsulated by a polymer for use as a marker in a SQUID magnetic sensor

influences the properties of the magnetic marker. In particular, the particles are 20 to 40 nm, which is larger than that of the commercially available or conventionally known magnetic fine particles. In this range, the magnetic fine particles can exhibit residual magnetism, for the enhancement of the magnetic signal. Smaller particles exhibit superparamagnetism.

Submitted herewith is a paper by the present inventors, (K. Enpuku, and K. Yoshinaga, et al., Jpn. J. Appl. Phys. Vol. 42 (2003) pp. L1436-L1438, Pt. 2, No. 12A). In that publication, a magnetic immunoassay with SQUID and a magnetic marker is disclosed. The remnance (the residual magnetism) due to an  $\text{Fe}_3\text{O}_4$  particle with a diameter of 25nm, was used for the detection (see Abstract and Fig. 3). Also submitted is another paper by the present inventors (K. Enpuku, and K. Yoshinaga, et al., IEEE Trans. Appl. Supercond., Vol. 13, pp. 371-376, 2003). In that publication, it is disclosed that an  $\text{Fe}_3\text{O}_4$  particle having a large diameter ( $d=25\text{nm}$ ) exhibits remnance (residual magnetism), while an  $\gamma$ -  $\text{Fe}_2\text{O}_3$  particle with a smaller diameter ( $d=10\text{nm}$ ) has a superparamagnetic property, i.e., it is free of residual magnetism (see section IV. MAGNETIC MARKER).

The Colin reference does not disclose or suggest a marker as presently claimed. Colin prefers that the metal core is free of residual magnetism and its mean size is between 5 and 30 nm, in particular, between 10 and 20nm (col. 3, lines 40-42). Thus, the metal particles described in Colin are similar, in many respects, to the commercially available or conventionally known magnetic particles discussed in the present application in which the diameter of the magnetic particle (metal core) is about 10 to 15nm, the external diameter of the assembly is 50 to 1000nm, and the detection is based on the superparamagnetism of the metal core. Colin discloses a device (1) which consists of a standard Mettler precision balance, under a top glass (2) of which is placed a magnet (3) 13 mm in diameter and 5 mm high. The magnet is integrally attached to a tray (4) of the balance through a nonmagnetic vertical axle (5). A container (6), which receives the sample to be determined, is placed on a sheet of aluminum placed over the magnet but without being in contact with it. A sample and a reagent (7) are brought into contact in the container (6). Such a system results in negative weighing values (col. 5, lines 33-35) due to the lightening of the tray when the metal clusters comprising superparamagnetic

particles are assembled by the magnet on the bottom of a container, due to the attractive force between the magnet and the metal particles (specially, the metal core).

Thus, it is clear that the method of Colin utilizes particles with a superparamagnetic or paramagnetic metal core, thereby avoiding residual magnetism. There is no disclosure or suggestion of detection of magnetic particles for residual magnetism (remnance) with a SQUID sensor. The metal particles disclosed in Colin would not serve as a highly-sensitive magnetic marker for use in measuring an immunoreaction with a SQUID magnetic sensor.

Accordingly, it is submitted that claim 1, and claims 2-6 dependent therefrom, distinguish patentably and unobviously over the Colin reference.

New claim 7 recites a combination of a SQUID magnetic sensor and a magnetic marker. The Colin reference does not disclose such a combination.

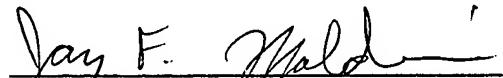
### CONCLUSION

For the reasons detailed above, it is respectfully requested all claims remaining in the application (Claims 1-7) are now in condition for allowance.

Respectfully submitted,

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April 19, 2006  
Date

  
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April <u>19</u> , 2006	Theresa L. Lucas 